IN THE CLAIMS

1 (Currently Amended). A method for the modulation of tissue-remodeling, the method comprising:

contacting the tissue to be remodeled with an effective amount of a compound comprising a sequence selected from the group consisting of:

(a) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 249 to 279 of TGFβI receptor (HJ loop);

(b) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 119 to 139 of TGFβI receptor (αD region);

(c) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 104 to 115 of TGFβI receptor (B4-B5 region);

(d) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 89 to 103 of TGFβI (A-region);

(e) a variant of a sequence according to any one of (a) to (d) wherein up to 40% of the amino acid of the native sequence have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic organic moiety; and/or up to 40% of the amino acids have their side chains chemically modified and/or up to 20% of the amino acids have been deleted; provided that at least 50% of the amino acids in the parent sequence of (a) to (d) are maintained unaltered in the variant, and provided that the variant maintains the biological activity of the parent sequences of (a) to (d);

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(f) a sequence of any one of (a) to (e) wherein at least one of the amino acids is replaced by the corresponding D-amino acid;

(g) a sequence of any one of (a) to (f) wherein at least one of the peptidic backbones has been

altered to a non-naturally occurring peptidic backbone;

(h) a sequence being the sequence of any one of (a) to (g) in reverse order; and

(i) a combination of two or more of the sequences of (a) to (h).

2 (Currently Amended). A method of Claim 1, wherein the TGFβ superfamily Ser/Thr receptor is selected from~~:~~ the group consisting of ALK1, TGFβRII, ACTRIIA, ALK3, ALK4, ALK6, BMPRII and ILK.

3 (Currently Amended). The method of Claim 1, wherein the compound is selected from the group consisting of the compounds present in Table 1 and denoted as: K048D801, K048D101, K048H101, KO48H102, K048H103, K048H104, K048H105, K048H106, K048H107, K048H901, K048B901, K093D801, K093D101, K093H101, K107H901; K095D801, K095H101, K095B901~~;~~, K098D801, K098D802, K098H101, K098H901, K098A101, K098B901~~;~~, K099D801~~;~~, K099H101, K099B901~~;~~, K116D102, K116D001, K116H801~~;~~ and K116B901 (SEQ ID NOs:1-31, respectively).

4 (Currently Amended). The method of Claim 1, wherein the sequences of 1(a) to 1(i) are selected from the group consisting of any one of SEQ ID NO:1 to SEQ ID NO. 59.

5 (Original). A method according to Claim 1, for modulation of bone growth wherein the tissue to be remodeled is bone.

6 (Original). A method according to Claim 5, wherein the modulation is increase of bone growth.

7 (Original). A method according to Claim 1, wherein the tissue to be remodeled is hair follicles and the modulation is of hair growth.

8 (Original). A method according to Claim 7, wherein the modulation is the inhibition of cessation of hair growth (alopecia).

9 (Original). A method according to Claim 8, wherein the cessation of hair growth is a result of radiotherapy or chemotherapy.

10 (Original). A method according to Claim 1, wherein the modulation is of collagen deposition.

11 (Original). A method according to Claim 10, wherein the collagen deposition is a result of injury to the tissue.

12 (Currently Amended). A method for the modulation of tissue remodeling in a subject comprising:

administering to the subject in need of such treatment a therapeutically effective amount of a compound comprising a sequence selected from the group consisting of:

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(a) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 249 to 279 of TGFβI receptor (HJ loop);

(b) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 119 to 139 of TGFβI receptor (αD region);

(c) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 104 to 115 of TGFβI receptor (B4-B5 region);

(d) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 89 to 103 of TGFβI (A-region);

(e) a variant of a sequence according to any one of (a) to (d) wherein up to 40% of the amino acid of the native sequence have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic organic moiety; and/or up to 40% of the amino acids have their side chains chemically modified and/or up to 20% of the amino acids have been deleted; provided that at least 50% of the amino acids in the parent sequence of (a) to (d) are maintained unaltered in the variant, and provided that the variant maintains the biological activity of the parent sequences of (a) to (d);

B2

(f) a sequence of any one of (a) to (e) wherein at least one of the amino acids is replaced by the corresponding D-amino acid;

(g) a sequence of any one of (a) to (f) wherein at least one of the peptidic backbones has been altered to a non-naturally occurring peptidic backbone;

(h) a sequence being the sequence of any one of (a) to (g) in reverse order; and

(i) a combination of two or more of the sequences of (a) to (h).

13 (Currently Amended). A method according to Claim 12, wherein the modulation of tissue-remodeling is for the treatment of a condition selected from~~:~~ the group consisting of ~~Alopecia~~alopecia, fibrosis, scarring, wound healing, bone healing, improvement of bone density, a ~~micro vascular~~microvascular disorder, prevention of adhesion formation, cancer, an immune related response, and adipose cell differentiation.

14 (Currently Amended). A method according to Claim 13, for the treatment of ~~Alopecia~~alopecia, wherein the TGFβ superfamily Ser/Thr kinase receptor is ~~selected from~~ ALK1 ~~and~~ or ALK2.

15 (Currently Amended). A method according to Claim 14, wherein the compound is selected from the group consisting of compounds designated in Table 1 as K048H101 (SEQ ID NO:3) and~~,~~ K098H901 (~~SEQ ID~~ NO:~~3 and~~ SEQ ID NO:10~~, respectively~~).

16 (Original). A method according to Claim 13, for the reduction of scarring wherein the TGFβ superfamily Ser/Thr kinase receptor is ALK1.

17 (Original). A method according to Claim 16, wherein the compound is designated in Table 1 as K048H101 (SEQ ID NO:3).

18 (Original). A method according to Claim 13, for the reduction of adhesion formation, wherein the TGFβ superfamily Ser/Thr kinase receptor is ALK3.

19 (Original). A method according to Claim 18, wherein the compound is designated in Table 1 as K098H901 (SEQ ID NO:22).

20 (Currently Amended). A method for the modulation of cell proliferation when the TGFβ superfamily Ser/Thr kinase receptor is ~~selected from~~ ALK4 or ALK3.

21 (Currently Amended). A method according to Claim 20, wherein the compound is selected from the group consisting of compounds designated in Table 1 as~~:~~ K099B901 (SEQ ID NO:27) and K098H101 (SEQ ID NO:21).

Q3

22 (Currently Amended). A method according to Claim 13, for the enhancement of bone healing, wherein the TGFβ superfamily Ser/Thr kinase receptor is selected from the group consisting of ACRIIA, ALK3 and ALK4.

23 (Currently Amended). A method according to Claim 22, wherein the compound is selected from ~~compouds~~ the group consisting of compounds designated in Table 1 as~~:~~ K095D801 (SEQ ID NO:16), K098H101 (SEQ ID NO:21), and K099B901 (SEQ ID NO:27).

24 (Currently Amended). A method according to Claim 13, for increasing bone density wherein the TGFβ superfamily

Ser/Thr kinase receptor is selected from the group consisting of ACRIIA, ALK3 and ALK4.

25 (Currently Amended). A method according to Claim 24, wherein the compound is selected from the group consisting of compounds designated in Table 1 as K095D801 (SEQ ID NO:16), K098H101 (SEQ ID NO:21), and K099B901 (SEQ ID NO:27).

26 (Original). A method according to Claim 1, wherein the compound is linear.

27 (Original). A method according to Claim 26, wherein the compound comprises a hydrophobic moiety at one of its terminals.

28 (Original). A method according to Claim 27, wherein the hydrophobic moiety is a hydrocarbon having 4 to 20 carbon atoms.

29 (Original). A method according to Claim 27, wherein the compound comprises the hydrophobic moiety conjugated to the N-terminal of any one of the sequences as defined in Claim 1(a) to 1(i).

30 (Original). A method according to Claim 27, wherein the compound comprises a hydrophobic moiety conjugated to Gly, present at the N-terminal of any one of the sequences as defined in Claim 1(a) to 1(i).

31 (Original). A method according to Claim 12, wherein the compound is linear.

32 (Original). A method according to Claim 31, wherein the compound comprises a hydrophobic moiety at one of its terminals.

33 (Original). A method according to Claim 32, wherein the hydrophobic moiety is a hydrocarbon having 4 to 20 carbon atoms.

34 (Original). A method according to Claim 32, wherein the compound comprises the hydrophobic moiety conjugated to the N-terminal of any one of the sequences as defined in Claim 1(a) to 1(i).

35 (Original). A method according to Claim 32, wherein the compound comprises a hydrophobic moiety conjugated to Gly, present at the N-terminal of any one of the sequences as defined in Claim 1(a) to 1(i).

36 (Original). A method according to Claim 1, wherein the compound is a hydrophobic moiety conjugated to the N-terminal of any one of the sequences as defined in Claim 1(a) to 1(i).

37 (Currently Amended). A ~~method for obtaining a~~ compound for the modulation of tissue-remodeling obtained by the method comprising:

Q4

(I) providing a plurality of candidate compounds comprising a sequence selected from:

(a) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 249 to 279 of TGFβI receptor (HJ loop);

(b) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 119 to 139 of TGFβI receptor ~~()~~ (αD region);

a4

(c) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 104 to 115 of TGFβI receptor (B4-B5 region);

(d) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 89 to 103 of TGFβI (A-region);

(e) a variant of a sequence according to any one of (a) to (d) wherein up to 40% of the amino acid of the native sequence have been replaced with a naturally or non-naturally occurring amino acid or with a peptidomimetic organic moiety; and/or up to 40% of the amino acids have their side chains chemically modified and/or up to 20% of the amino acids have been deleted; provided that at least 50% of the amino acids in the parent sequence of (a) to (d) are maintained unaltered in the variant, and provided that the variant maintains the biological activity of the parent sequences of (a) to (d);

Q4

(f) a sequence of any one of (a) to (e) wherein at least one of the amino acids is replaced by the corresponding D-amino acid;

(g) a sequence of any one of (a) to (f) wherein at least one of the peptidic backbones has been altered to a non-naturally occurring peptidic backbone;

(g) a sequence being the sequence of any one of (a) to (g) in reverse order; and

(i) a combination of two or more of the sequences of (a) to (h).

(II) assaying the candidate compounds obtained in (I) in a test assay for tissue remodeling, and determining the level of tissue-remodeling of each candidate compounds;

Q4

(III) selecting those compounds which modulate tissue remodeling as compared to the tissue remodeling in the same test assay in the absence of the candidate compounds, thereby obtaining compounds being capable of modulating tissue remodeling activities.

Cancelled

38 (Cancelled)

39 (Currently Amended). A ~~method~~ compound according to claim 37, wherein step (i) comprises:

(i) determining which specific member of the TGFβ superfamily Ser/Thr kinase receptor is involved in the remodeling of the tissue to be modulated, and determining the sequence of the specific member from a database of amino acid sequences;

Q5

(ii) aligning the sequence of the catalytic unit of the member obtained in (i) with the sequence of the catalytic unit of TGFβI receptor-, and determining the sequence of the specific member in four regions corresponding, in the alignment, to the following, positions of TGFβI: 249 to 279 (HJ-loop), 119 to 139 (αD region), 104 to 115 (B4-B5 region), 250 to 265 (A-region);

(iii) determining a continuous stretch of at least 5 amino acids of any of the four regions of (ii) above that is sorter than the length of the full region and has modeling activities of the tissue-remodeling/ or TGFβ-kinase associated signal transduction, by: synthesizing a plurality of subsequences, optionally partially overlapping subsequences, of 5-10 mer from any of the above four regions; testing those sequences in a test assay for determining tissue-remodeling /or TGFβ-associated signal transduction, modulating activities, and selecting those sequences that have tissue remodeling/ or TGFβ-associated signal transduction modulating activities;

(iv) determining in the sequences of (ii) or in the sequences selected in (iii) above, essential and non-essential amino acids by: preparing a plurality of modified sequences wherein in each sequence a single and different position in the native sequence has been replaced with a test amino acid; testing those modified sequences in a test assay for determining tissue-remodeling /or TGFβ-associated signal transduction modulating activities; those amino acids which when replaced caused a statistically significant change in tissue-remodeling/TGFβ-associated signal transduction modulating activity being essential amino acids, and those amino acids which when replaced, did not cause a statistically significant change in tissue remodeling/TGFβ-associated signal transduction modulating activity, being non-essential amino acids;

a5

(v) preparing a plurality of compounds comprising sequences selected from the group consisting of:

(1) the sequences of (ii);

(2) the sequences selected in (iii);

(3) the sequences of (ii) or the selected sequence of (iii), wherein at least one of the essential amino acids has been replaced by a conservatively substituted naturally or non-naturally occurring amino acid, or a conservative peptidomimetic organic moiety; and/or at least one of the non-essential amino acids has been deleted, or substituted (conservatively or non-conservatively) by naturally or non-naturally occurring amino acids or a peptidomimetic;

(4) the sequences of (1) to (3) in a reverse order;

(5) the sequence of (4) wherein all the amino acids have been replaced by their D-counterpart residues;

said compounds of (v) being candidate compounds for modulating tissue remodeling.

40 (Cancelled)

41 (Currently Amended). A pharmaceutical composition comprising as an active ingredient the compound of Claim ~~40~~37.

42 (Original). A pharmaceutical composition comprising as an active ingredient two different compounds of Claim 40.

43 (Original). A pharmaceutical composition according to Claim 41, for the treatment of a disease or condition, wherein a beneficial effect is evident by the modulation of tissue-remodeling.

44 (Currently Amended). A pharmaceutical composition according to Claim 43, for the treatment of a disease or condition selected from~~:~~ the group consisting of ~~Alopecia~~alopecia, fibrosis, scarring, wound healing, bone healing, improvement of bone density, a ~~micro vascular~~microvascular disorder, adhesion formation, cancer, an immune related response, and adipose cell differentiation.

Q7

45 (Currently Amended). A ~~method for obtaining compounds~~compound for the modulation of tissue remodeling, comprising:

(I) providing a plurality of candidate compounds comprising a sequence selected from:

(a) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor

corresponding to positions 249 to 279 of TGFβI receptor (HJ loop);

(b) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 119 to 139 of TGFβI receptor (αD region);

(c) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 104 to 115 of TGFβI receptor (B4-B5 region);

(d) a sequence which is a continuous stretch of at least five amino acids present in a native TGFβ superfamily Ser/Thr kinase receptor, in positions of the receptor corresponding to positions 89 to 103 of TGFβI (A-region);

(e) a variant of a sequence according to any one of (a) to (d) wherein up to 40% of the amino acid of the native sequence have been replaced with a naturally or non-

naturally occurring amino acid or with a peptidomimetic organic moiety; and/or up to 40% of the amino acids have their side chains chemically modified; and/or up to 20% of the amino acids have been deleted, provided that at least 50% of the amino acids in the parent sequence of (a) to (d) are maintained unaltered in the variant, and provided that the variant maintains the biological activity of the parent sequences of (a) to (d);

a7

(f) a sequence of any one of (a) to (e) wherein at least one of the amino acids is replaced by the corresponding D-amino acid;

(g) a sequence of any one of (a) to (f) wherein at least one of the peptidic backbones has been altered to a non-naturally occurring peptidic backbone;

(h) a sequence being the sequence of any one of (a) to (g) in reverse order; and

(i) a combination of two or more of the sequences of (a) to (h).

(j) contacting the candidate compounds with a test assay for determining the level of a physiological property mediated through a TGFβ superfamily Ser/Thr kinase receptor signal transduction;

(i) selecting those compounds which modulate the level of the physiological property in the test assay as compared to the modulation of the level of signal transduction in the same test assay in the absence of the candidate compound;

a7

(II) contacting the compounds selected in (III) with a test assay for determining the level of tissue remodeling;

(III) selecting those compounds which modulate tissue-remodeling as compared to the tissue-remodeling in the same test assay in the absence of the candidate compounds, thereby obtaining compounds being capable of modulating kinase activity.

46 (Cancelled)

47 (Currently Amended). A ~~method~~ compound according to claim 45, wherein said step (i) comprises:

a8

(i) determining which specific member of the TGFβ superfamily Ser/Thr kinase receptor is involved in the remodeling of the tissue to be modulated, and determining the sequence of the specific member from a database of amino acid sequences;

(ii) aligning the sequence of the catalytic unit of the member obtained in (i) with the sequence of the catalytic unit of TGFβI receptor—, and determining the sequence of the specific member in four regions corresponding, in the alignment, to the following, positions of TGFβI: 249 to 279 (HJ-loop), 119 to 139 (αD region), 104 to 115 (B4-B5 region), 250 to 265 (A-region);

(iii) determining a continuous stretch of at least 5 amino acids of any of the four regions of (ii) above that is sorter than the length of the full region and has modeling activities of the tissue-remodeling/ or TGFβ-kinase associated signal transduction, by: synthesizing a plurality of subsequences, optionally partially overlapping subsequences, of 5-10 mer from any of the above four regions;

testing those sequences in a test assay for determining tissue-remodeling /or TGFβ-associated signal transduction, modulating activities, and selecting those sequences that have tissue remodeling/ or TGFβ-associated signal transduction modulating activities;

(iv) determining in the sequences of (ii) or in the sequences selected in (iii) above, essential and non-essential amino acids by: preparing a plurality of modified sequences wherein in each sequence a single and different position in the native sequence has been replaced with a test amino acid; testing those modified sequences in a test assay for determining tissue-remodeling /or TGFβ-associated signal transduction modulating activities; those amino acids which when replaced caused a statistically significant change in tissue-remodeling/TGFβ-associated signal transduction modulating activity being essential amino acids, and those amino acids which when replaced, did not cause a statistically significant change in tissue remodeling/TGFβ-

associated signal transduction modulating activity, being non-essential amino acids;

(v) preparing a plurality of compounds comprising sequences selected from the group consisting of:

(1) the sequences of (ii);

(2) the sequences selected in (iii);

(3) the sequences of (ii) or the selected sequence of (iii), wherein at least one of the essential amino acids has been replaced by a conservatively substituted naturally or non-naturally occurring amino acid, or a conservative peptidomimetic organic moiety; and/or at least one of the non-essential amino acids has been deleted, or substituted (conservatively or non-conservatively) by naturally or non-naturally occurring amino acids or a peptidomimetic;

a8

(4) the sequences of (1) to (3) in a reverse order;

(5) the sequence of (4) wherein all the amino acids have been replaced by their D-counterpart residues;

said compounds of (v) being candidate compounds for modulating tissue remodeling.

48 (Cancelled)

49 (Currently Amended). A pharmaceutical composition comprising as an active ingredient the compound of Claim ~~48~~45.

50 (Currently Amended). A pharmaceutical composition comprising as an active ingredient two different compounds of Claim ~~48~~45.

51 (Original). A pharmaceutical composition according to Claim 49, for the treatment of a disease or condition, wherein a beneficial effect is evident by the modulation of tissue-remodeling.

52 (Currently Amended). A pharmaceutical composition according to Claim 51, for the treatment of a disease or condition selected from~~:~~ the group consisting of ~~Alopecia~~alopecia, fibrosis, scarring, wound healing, bone healing, improvement of bone density, a ~~micro vascular~~microvascular disorder, adhesion formation, cancer, an immune related response, and adipose cell differentiation.

53 (Cancelled).

54 (Currently Amended). A pharmaceutical composition comprising as an active ingredient the compound of Claim ~~53~~39.

55 (Currently Amended). A pharmaceutical composition comprising as an active ingredient two different compounds of Claim ~~53~~39.

Q11

56 (Original). A pharmaceutical composition according to Claim 54, for the treatment of a disease or condition, wherein a beneficial effect is evident by the modulation of tissue-remodeling.

57 (Currently Amended). A pharmaceutical composition according to Claim 56, for the treatment of a disease or condition selected from~~:~~ the group consisting of ~~Alopecia~~alopecia, fibrosis, scarring, wound healing, bone healing, improvement of bone density, a ~~micro vascular~~microvascular disorder, adhesion formation, cancer, an immune related response, and adipose cell differentiation.

Q12

58 (Cancelled).

59 (Currently Amended). A pharmaceutical composition comprising as an active ingredient the compound of Claim ~~58~~47.

60 (Currently Amended). A pharmaceutical composition comprising as an active ingredient two different compounds of Claim ~~58~~47.

Q13

61 (Original). A pharmaceutical composition according to Claim 59, for the treatment of a disease or

condition, wherein a beneficial effect is evident by the modulation of tissue-remodeling.

62 (Currently Amended). A pharmaceutical composition according to Claim 60, for the treatment of a disease or condition selected from~~:~~ the group consisting of ~~Alopecia~~alopecia, fibrosis, scarring, wound healing, bone healing, improvement of bone density, a ~~micro vascular~~microvascular disorder, adhesion formation, cancer, an immune related response, and adipose cell differentiation.

63 (Currently Amended). A method for the modulation of tissue-remodeling, the method comprising contacting the tissue to be remodeled with an effective amount of a compound of Claim ~~40~~37.

a14

64 (Currently Amended). A method for the modulation of tissue-remodeling, the method comprising contacting the tissue to be remodeled with an effective amount of a compound of Claim ~~48~~45.

65 (Currently Amended). A method for the modulation of tissue-remodeling, the method comprising contacting the tissue to be remodeled with an effective amount of a compound of Claim ~~53~~39.

66 (Currently Amended). A method for the modulation of tissue-remodeling, the method comprising contacting the

tissue to be remodeled with an effective amount of a compound

Q14 | of Claim ~~5847~~.